Alerts, Notices, and Case Reports

Fatal Salicylate Toxicity From Bismuth Subsalicylate

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FATAL SALICYLATE INGESTION usually results from concentrated formulations of salicylates found in analgesics, cold and sinus medications, and aspirin-containing topical compounds.

I describe a case of salicylate toxicity leading to death secondary to the abuse of Pepto-Bismol, whose active and toxic ingredient is bismuth subsalicylate.

Report of a Case

The patient, an 82-year-old previously healthy woman, presented to the Riverside (California) Community Hospital Emergency Department with an altered level of consciousness, according to her son with whom she was living. In the previous 24 hours, she had exhibited slurred speech, lethargy, and a decreased oral intake. Her son also reported that for several days she had complained of an exacerbation of her chronic abdominal pain. As a result, she had been ingesting large amounts of Pepto-Bismol tablets daily, including 66 tablets in the 24 hours before admission. There was no history of nausea or vomiting. Stools had been watery and black for several days.

Her medical history was significant for chronic abdominal pain that remained undiagnosed despite extensive evaluations in the past. She had not seen a physician in several years. Current medications included only Pepto-Bismol. She was allergic to codeine.

On her initial examination, this frail, small-of-stature elderly woman was confused and lethargic. Her supine blood pressure was 118/70 mm of mercury with a pulse rate of 70 per minute, a respiratory rate of 20, and a temperature of 37°C (98.6°F); she weighed 36 kg (79 lb). Her skin was warm and dry with tenting. Mucous membranes were dry. Auscultation of her lungs revealed rales at the left base. The abdomen displayed no palpable mass, rebound, guarding, or organomegaly. On rectal examination, the stool was dark brown and guaiac-negative. On neurologic examination, she was disoriented in all spheres and lethargic.

The following laboratory values were obtained: hemoglobin 111 grams per liter (11.1 grams per dl); hematocrit 0.32; leukocyte count 11.2×10^9 per liter (11,200 per μl), with 0.87 neutrophils, 0.06 bands, and 0.06 lymphocytes; sodium 143, potassium 3.5, chloride 108, and carbon dioxide content 16 mmol per liter; blood urea nitrogen 1.0 mmol per liter (28 mg per dl); creatinine 97 μmol per liter (1.1 mg per dl); prothrombin time 15.5 seconds (control 11 to 13); partial prothrombin time 30.2 seconds (control 20 to 30); and glucose level 6.0 mmol per liter (108 mg per dl). Arterial blood gas determinations with the patient receiving 2 liters of oxygen showed a pH of 7.55, a P_{CO_2} of 14 mm of mercury, and a P_{O_2} of 160 mm of mercury, consistent with a mixed respiratory alkalosis and metabolic acidosis. A salicylate level was 46 mg per dl.

Other studies included a normal electrocardiogram and upright chest radiograph. A plain film of the abdomen revealed pronounced densities in the bowel, consistent with "barium or some other radio-opaque substance," according to the radiologist's interpretation (Figure 1). Computed tomography of the head showed diffuse cortical atrophy.

The patient was admitted to the care of her family practitioner with a diagnosis of dehydration, encephalopathy, and salicylate toxicity due to Pepto-Bismol abuse. Despite hydration and urinary alkalinization over the next two days, her condition continued to deteriorate, and she had progressively lower hematocrits, higher leukocyte counts, and steady salicylate levels and anion gaps. A gastroscopy revealed mild generalized intestinal inflammation but no focal bleeding. Three days after admission, her hematocrit was 0.19, a salicylate level was 20 mg per dl, and the anion gap was 24. She died of pulmonary edema on the same day.

Discussion

As a result of safety packaging and the rise of acetaminophen use as an antipyretic in children, there has been a dramatic decrease in the incidence of salicylate deaths in children over the past several years.[1] Yet, aspirin remains as a relatively common source of poisoning in adults. Integrated into more than 200 different formulations (probably more than any other drug), salicylates are commonly overlooked by patients and physicians alike as a source of potential toxicity (Table 1).[2-4]

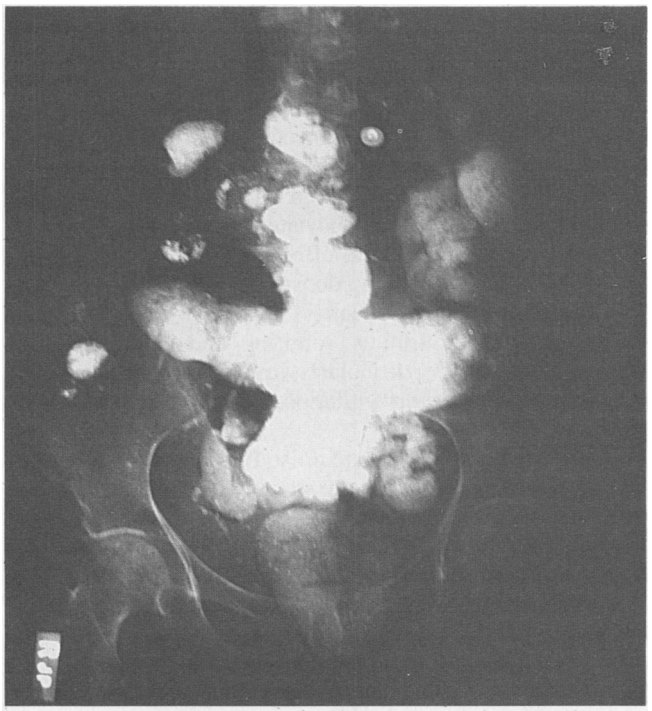

Figure 1.—A plain film of the abdomen shows pronounced densities in the bowel.

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TABLE 1.—*Common Sources of Salicylates*

Selected Formulations (Manufacturer)	*Generic and Chemical Name*
Prescription	
Darvon Compound (Eli Lilly and Co)	Propoxyphene HCl, aspirin, and caffeine
Empirin with Codeine (Burroughs Wellcome)	Aspirin and codeine phosphate
Fiorinal (Sandoz)	Butalbital, aspirin, and caffeine
Percodan (DuPont)	Oxycodone HCl, oxycodone terephthalate, and aspirin
Over-the-Counter	
Aspirin tablets and suppositories (numerous preparations)	--
Alka-Seltzer (Miles Inc)	Aspirin, sodium bicarbonate, citric acid, sodium citrate, and sodium salicylate
Ascriptin (Rhone-Poulenc Rorer)	Aspirin, magnesium hydroxide, dried aluminum hydroxide gel, and calcium carbonate
Aspercreme (Thompson Medical)	Topical cream containing trolamine salicylate
Ben-Gay External Analgesic (Pfizer)	Topical cream containing methyl salicylate and menthol
Bufferin (Bristol-Myers)	Aspirin, calcium carbonate, magnesium oxide, and magnesium carbonate
Cope (Glenbrook)	Aspirin and caffeine
Dristan (Whitehall)	Phenylephrine HCl, chlorpheniramine maleate, and acetaminophen
Ecotrin (SmithKline Beecham)	Enteric-coated aspirin
Excedrin (Bristol-Myers)	Acetaminophen, aspirin, and caffeine
Midol (Glenbrook)	Acetaminophen, pamabrom, and pyrilamine maleate
Oil of wintergreen	Methyl salicylate
Pepto-Bismol (Procter & Gamble)	Bismuth subsalicylate
Sine-Aid (McNeil)	Acetaminophen and pseudoephedrine HCl
Triaminicin (Sandoz)	Phenylpropanalamine HCl and chlorpheniramine maleate
Vanquish (Glenbrook)	Aspirin, acetaminophen, caffeine, dried aluminum hydroxide gel, and magnesium hydroxide

HCl = hydrochloride

The elderly in particular are at high risk for both accidental and chronic salicylate poisoning.[5] Presenting frequently with an altered sensorium, they can prompt a fruitless search for a primary neurologic cause, delaying critical treatment of their toxic syndrome. Even when salicylates are identified as the source of a patient's illness, determining the degree of toxicity is difficult. The usefulness of the Done nomogram is currently unclear, and it is certainly invalid in cases of chronic toxicity, with the use of enteric-coated preparations, and when there is delayed gastric emptying or salicylate concretions.[4,6]

Salicylates uncouple oxidative phosphorylation and inhibit dehydrogenases and aminotransferases, leading to a rise in organic anions and metabolic acidosis. They also stimulate the respiratory system, resulting in hyperventilation and respiratory alkalosis. This in turn leads to the renal excretion of bicarbonate and potassium. Larger doses can depress respirations. Hypothrombinemia and platelet dysfunction are common complications of salicylate toxicity, producing prolonged bleeding times. Other effects are diaphoresis and hyperthermia, each worsening dehydration.[1,4]

The clinical features of salicylate toxicity are hyperpnea, confusion, lethargy, tinnitus, vomiting, and abdominal pain. Signs include fever (particularly in children), diaphoresis, dehydration, and hyperventilation. Coma indicates a poor prognosis.[1,4,7]

The treatment of salicylate poisoning is challenging. Despite their dehydration, many patients are predisposed to noncardiogenic pulmonary edema. Forced alkaline diuresis, the cornerstone of emergency department therapy, can worsen this condition. Excessive bicarbonate administration to increase the renal excretion of salicylates or to correct the salicylate-induced metabolic acidosis can lead to equally dangerous alkalinemia. Hemodialysis can be effective in eliminating salicylates, but its use should be reserved for severely poisoned patients.[1,4,8]

The patient in this report had most of the classic features of salicylate poisoning. She presented with dehydration and central nervous system dysfunction. Examination revealed acid-base and clotting disorders, with progressive central nervous system depression, anemia, pulmonary edema, and eventually death. Because of long-term salicylate use, in the form of enteric-coated tablets, the salicylate level underestimated both the degree and likelihood of the progression of toxicity.

What is atypical is the source of the salicylate: Pepto-Bismol tablets, each of which contains 262 mg of bismuth subsalicylate and 102 mg of available salicylate.[9] The recommended dosing schedule—2 tablets orally four times a day—would deliver 11.6 mg of salicylate per kilogram per day in a 70-kg adult, less than 3 mg per kg per dose. In this case study, the ingestion of 66 tablets by a 36-kg patient resulted in a dose of 187 mg per kg—taken in conjunction with probable underlying long-term salicylate abuse. Although mentioned frequently in the literature as a source of absorbable salicylate, Pepto-Bismol use has not been reported in an actual death from salicylate toxicity.[9-11]

The key to effective intervention in salicylate toxicity remains the prompt recognition of its existence, whether it be accidental, suicidal, or iatrogenic.

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Ciguatera Fish Poisoning in San Francisco, California, Caused by Imported Barracuda

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CIGUATERA FISH POISONING is endemic to tropical waters, where reef-dwelling fish ingest toxins produced by the dinoflagellate *Gambierdiscus toxicus*. The disease, which is caused by the ingestion of fish contaminated with ciguatera toxins, produces gastrointestinal and neurologic symptoms. These consist of an early gastrointestinal phase (abdominal pain, vomiting, diarrhea) followed by a neurologic or constitutional phase (pruritus, muscle pain, weakness, "burning tongue," blurred vision, dizziness, headache, and hot-cold reversal). We report an outbreak of ciguatera poisoning that occurred in 1989 in San Francisco, California, caused by barracuda (*Sphyraena* species) imported from Florida. This disease is rare in California, having previously been reported in Monterey, California (caused by mullet imported from Florida), and in the San Francisco Bay Area (jack fish from Midway Island).[1]

Reports of Cases

Four members of a Vietnamese-American family became ill after sharing a meal. The family included a 54-year-old man, a 53-year-old woman, their 21-year-old daughter, and 24-year-old son. All patients were in good health before the meal, which consisted of fresh corn on the cob, commercially canned mushrooms, and steamed fish. Only the fish was eaten by all four people. No shellfish had been ingested.

The fish was said to be a "nhong" fish, described as 1.2 m (4 ft) long with a pointed snout. It was purchased from an open-air farmers' market in San Francisco. The family purchased and ate only the head of the fish, which they said was large and contained abundant flesh. Investigation by the county health department determined that the fish eaten was from a shipment of frozen barracuda flown in from Fort Pierce, Florida, and apparently sold to several Asian-American families.

(Geller RJ, Olson KR, Senécal PE: Ciguatera fish poisoning in San Francisco, California, caused by imported barracuda. West J Med 1991 Dec; 155:639-642)

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Case 1

At five hours, the father complained of weakness, burning of the tongue, and blurred vision. He became profoundly weak and by eight hours could not get up off the floor. He had no nausea, vomiting, or diarrhea. Paramedics found the patient prostrate with a pulse of 40 beats per minute and a systolic pressure of 80 mm of mercury. He did not have chest pain, and there were no signs of heart failure. Atropine sulfate, 0.5 mg, was administered intravenously (IV). Twenty minutes later, his blood pressure was 132/52 mm of mercury, and his pulse was 88 beats per minute.

In the Emergency Department at San Francisco General Hospital, he had numbness to the face and extremities, weakness, and periumbilical abdominal pain. His blood pressure was 144/90 mm of mercury, pulse rate 84 beats per minute, and he was afebrile. Initial laboratory values included a leukocyte count of 9.0×10^9 per liter (9,000 per μl), hemoglobin 120 grams per liter (12.0 grams per dl), and hematocrit 0.37 (37%). The serum glucose level was 12.7 mmol per liter (229 mg per dl), blood urea nitrogen 7.9 mmol per liter (22 mg per dl), and creatinine 106.1 μmol per liter (1.2 mg per dl). Serum sodium was 139, potassium 3.3, chloride 103, and bicarbonate 27 mmol per liter. Arterial blood gas determinations with the patient receiving supplemental oxygen showed a Po_2 of 344 mm of mercury, a Pco_2 of 44.8 mm of mercury, and pH 7.35.

Because of abdominal pain, a surgical evaluation was done. Bradycardia and hypotension recurred, but additional atropine was not given. Instead, fluid administration was begun. After six hours, he had received 4,000 ml of fluid IV and his systolic blood pressure had still fallen to 70 mm of mercury, with a pulse of 54 beats per minute. An abdominal x-ray series was initially read as showing free air under the diaphragm. A subsequent exploratory laparotomy revealed no intra-abdominal disease.

His hospital course was remarkable for persistent weakness, recurrent bradycardia, and hypotension. His pulse rate stayed between 45 and 55 beats per minute with systolic blood pressures in the range of 80 to 90 mm of mercury. He tolerated these values generally without symptoms and was discharged after nine days.

Two days later, he was readmitted with severe pruritus unresponsive to the administration of diphenhydramine hydrochloride, which had led to a significant cellulitis around his buttocks and presacral area due to excoriation. Mild orthostatic changes in pulse and blood pressure were noted but did not cause symptoms.

Case 2

At 12 hours, the mother became ill in the emergency department while waiting for her husband. She complained of fatigue, nausea, and chest pain. Initially her pulse rate was 68 beats per minute and her blood pressure was 132/90 mm of mercury. At 18 hours, she had nausea and vomiting and complained that her face and throat felt swollen. Her blood pressure was then noted to be 80/38 mm of mercury, and her pulse was 60 beats per minute. Thereafter, her pulse and blood pressure remained low.

Initial laboratory tests revealed a leukocyte count of 11.6×10^9 per liter (11,600 per μl), with 0.69 granulocytes and 0.27 lymphocytes; hemoglobin 122 grams per liter; and hematocrit 0.375. Serum sodium was 141, potassium 3.8,